

Dr. Joshua Lederberg, President The Rockefeller University New York, NY 10021

Dear Josh:

Thanks for your note and the reprints of your Commentary on the human genome project and the Perspectives on replica plating and indirect selection. And apologies for the delay in this reply.

Your views on the human genome project make excellent sense and I cannot understand the enthusiasm of some people. It is surely the least cost-effective and probably the slowest way of getting an understanding of the working of the human genome. It is remindful of the issue 30 years ago of how best to explore space - with humans aboard or not. The same kind of forces that determined that decision again seem operative. Not only do we see large Federal labs bidding for a piece of the action but also already I had a call from an aerospace company asking about some collaboration with our Institute. Recently I have seen a lot of questioning of the use of humans in our space missions. It may take another 30 years before the poor wisdom of the human genome project is appreciated.

You were generous in your reference in your Perspectives to our replica plating system. For my part, the interest was in a set-up where we could make replicate prints of a matrix of colonies onto a variety of test plates. Its use for indirect selection of mutants did not occur to me, perhaps because I had not been thinking of something with the resolving power of velveteen.

When I first heard of Cairns recent work I was less skeptical than if it had come from someone whom I respected much less. Whether he is correct or not in the example he reported I am undecided. But it has since occurred to me that given the enormous evolutionary potential of microorganisms and given the great advantage of competence for post-adaptive mutation, that bacteria may have achieved that ability in a few cases. On the other hand the advantage may not be so great after all. In effect, post-adaptive mutation would represent an increase by a factor of 10⁵-10⁸ over spontaneous rates. Even these apparently large factors may not be large enough to offer the necessary selective advantage. In any event, post-adaptive mutation along with cold fusion has enlivened things, even if unreal.

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By the way did you notice the review article in Nature on organic carbon in sedimentary rocks over the last 3,800 million years (Schidlowski, Nature 333, 313-318, 1988). On the basis of $^{13}\text{C}/^{12}\text{C}$ comparisons he concluded that life was present almost 4 billion years ago and in an abundance no less than that today. Carbon in contemporary life is poorer in ^{13}C than in carbonate. But I do not believe he can exclude that the ancient carbon came from abiotic synthesis. I cannot understand why the relative abundance has remained constant. His assumption that it has been the result of limitation by something like phosphate.

It was very good to hear from you and I hope I get to see you again soon.

Best regards.

Aaron Novick

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